Double-stranded RNA adenosine deaminase ADAR1 enhances both T cell susceptibility to human T-cell leukemia virus type 1 and 2 and viral replication

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Cachat et al. Retrovirology 2014, 11(Suppl 1):O49
http://www.retrovirology.com/content/11/S1/O49

RETROVIROLOGY

ORAL PRESENTATION Open Access

Double-stranded RNA adenosine deaminase ADAR1 enhances both T cell susceptibility to human T-cell leukemia virus type 1 and 2 and viral replication

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From 16th International Conference on Human Retroviruses: HTLV and Related Viruses
Montreal, Canada. 26-30 June 2013

Type I interferons represent the first line of defense against pathogens. This family of cytokines activates the expression of antiviral proteins, such as the protein kinase R (PKR), an inhibitor of viral mRNA translation, and the double-stranded RNA adenosine deaminase ADAR1. ADAR1 has the ability to convert adenosine (A) into guanosine (G), thereby introducing mutations in the viral genome during its replication. A to G editing was previously reported in cells expressing HTLV-2 or STLV-3 viruses but not investigating in HTLV-1 expressing cells (Ko et al. J. Gen Virol. 2013). Consequently we investigated whether ADAR1 expression was associated or not with an antiviral effect in the course of HTLV-1 and HTLV-2 infections. We first show that ADAR1 expression is increased in ATL patient peripheral blood mononuclear cells, in HTLV-1 and HTLV-2 transformed cell lines as well as in activated primary peripheral blood lymphocytes. Strikingly, in cells transfected with HTLV-1 and HTLV-2 molecular clones, ADAR1 over-expression enhances viral replication and viral egress through PKR functional inhibition, as demonstrated by western-blot analyses, luciferase assays, ELISA and infection experiments. We also demonstrate that this effect is independent of ADAR catalytic activity. In addition, ADAR1 expression enhances the susceptibility of a non-infected T cell line to HTLV-1 and HTLV-2 infection. Altogether, our results demonstrate that an interferon-induced protein exerts a proviral role in the context of HTLV infection by enhancing cells susceptibility to infection and increasing viral replication.

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Published: 7 January 2014

doi:10.1186/1742-4690-11-S1-O49
Cite this article as: Cachat *et al.*: Double-stranded RNA adenosine deaminase ADAR1 enhances both T cell susceptibility to human T-cell leukemia virus type 1 and 2 and viral replication. *Retrovirology* 2014 **11** (Suppl 1):O49.

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